AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning on page 5, line 27, to read as follows:

The membrane disruptive agent is a hydrophobic polymer (or at least is more hydrophilic than hydrophobic at a define pH, such as pH 7, as compared to a lower pH, such as pH 5), which in the preferred embodiment is designed to be stable and inert at physiologic conditions and to become both endoosomolytic and drug-releasing as the pH drops within the endosome. The membrane disruptive agent may be a hydrophobic polymer which is coupled to a hydrophilic polymer or multiple hydrophilic groups which are released after endocytosis to expose the hydrophobic polymer or a hydrophilic polymer which is protonated after endocytosis to yield a hydrophobic polymer, all of which are membrane disruptive. The hydrophilic components are preferably coupled to the ~~hydrophilic~~ hydrophobic component via a degradable linkage, most preferably an acid labile linkage which is cleaved following endocytosis. In one embodiment, the membrane disruptive agent is coupled to hydrophilic groups in an amount effective to make the polymer soluble in an aqueous solution and allow passage through the cell wall of the polymer. The hydrophilic groups are coupled to the polymeric backbone via linkages that are disrupted upon exposure to an appropriate stimulus, typically a change in pH, and most typically a decrease in pH from physiological pH (i.e., typically pH 7.4) to the pH of the endosome (approximately between 5 and 6.5). With the removal of the hydrophilic groups, the polymer again becomes hydrophobic and disrupts the endosomal membrane, releasing the endosomal contents into the cytoplasm.

Please amend the paragraph beginning on page 28, line 18, to read as follows:

These materials can be coupled to the conjugate using standard chemical techniques, or in some cases, using recombinant technology, for example, to make a fusion protein. ~~AUTHOR (I~~

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS PLLC
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100

~~have no idea)~~ Wilder et al., *J. Clin. Oncol.* 14:1383-1400 (1996). Covalent linkages can be formed using chemical reactions well known to those of skill in the art. For example, glycoproteins often have saccharide moieties, which can be oxidized to provide aldehyde groups. Aldehyde groups are known to react with amines to form Schiff bases, which can then be reduced with sodium cyanoborohydride in a process known as reductive amination. Peptides which have amine groups and carboxylic acid groups, polymers with carboxylic acid groups, and polymers and peptides with imidazole groups and other groups which hydrolyze phospholipid membranes at the pH range within the endosomes can be covalently coupled using methods well known to those of skill in the art. The agent can be coupled via a degradable linkage, such as an acetal, anhydride, ester, orthoester, amide, Schiff base or disulfide linkage, or a stimuli disruptible linkage, as discussed above in section IIIb. In the preferred embodiment, these linkages are acid degradable, as discussed in the foregoing section IIIa.

LAW OFFICES OF
CHRISTENSEN O'CONNOR JOHNSON KINDNESS^{PLLC}
1420 Fifth Avenue
Suite 2800
Seattle, Washington 98101
206.682.8100